B cont'd.

74. The method of claim 73 wherein the disease or condition is neuropathic pain.

Please substitute the claim set in the appendix entitled Clean Version of Pending Claims for the previously pending claim set. The substitute claim set is intended to reflect cancellation of claims1-39 and addition of new claims 40-74.

REMARKS

Claims 1-39 have been cancelled and 40-74 have been added. Examination of the claims 40-74 is respectfully requested.

No new matter was added by these amendments. For the Examiner's convenience, it is noted that claim 40 is original claim 18; claim 41 is original claims 34 and 35; claim 42 is original claim 29; claim 43 is original claim 30; claim 44 is supported by original claim 34 and the specific value for Y provided in the specification at page 42, line 5; claim 45 is supported by original claim 35 and the specific value for Y provided in the specification at page 42, line 5; claims 46-61 are supported by original claims 2-17; claims 62-63, 64-69, 70 and 71 are supported by original claims 19-20, 22-27, 31, and 36; and claims 72-74 are supported by original claims 37-39.

The Examiner is invited to telephone Applicants' undersigned attorney if there are any questions concerning this application.

Respectfully submitted,

JASON P. CHINN ET AL.

By their Representatives,

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Date 6-11-02 By _____
Robert J. Harris, Ph.D.
Reg. No. 37,346

CERTIFICATE UNDER 37 CFR 1.8: The undersigned hereby certifies that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail, in an envelope addressed to: Commissioner of Patents, Washington, D.C. 20231, on this 11th day of June, 2002.

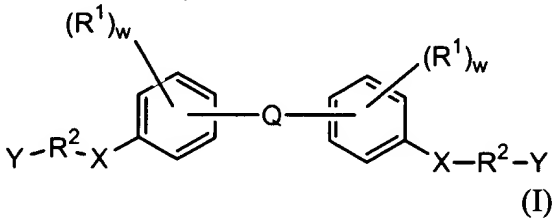
Dawn M. Poole
Name

Dawn M. Poole
Signature

Clean Version of Pending Claims

SODIUM CHANNEL MODULATORS
Applicant: Jason P. Chinn et al.
Serial No.: 09/943,420

40. A compound of formula I:



(I)

wherein:

Q is -O-, -$S(O)_m$-, -$(CR^5R^6)_p$-, -$O(CR^5R^6)_rO$-, or -$N(R^k)$-;

each R^1 is independently alkyl, alkenyl, alkynyl, aryl, heteroaryl, cycloalkyl, heterocyclyl, or R^a;

each R^2 is independently a covalent bond or alkylene; wherein alkylene is optionally substituted with 1 to 4 substituents independently selected from R^b;

each X is independently oxy (-O-) or -$N(R^m)$-;

each Y is independently a heterocyclyl containing at least one nitrogen atom, wherein each nitrogen of the heterocyclyl is substituted with R^3 and wherein each heterocycle of Y is optionally substituted with 1, 2, 3, or 4 substituents independently selected from R^4;

each R^3 is independently hydrogen, alkyl, alkenyl, alkynyl, aryl, heteroaryl, cycloalkyl, oxo, or heterocyclyl; and each R^4 is independently alkyl, alkenyl, alkynyl, aryl, heteroaryl, cycloalkyl, heterocyclyl, or R^b; or R^3 and R^4 are joined to form a C_{1-4} alkylene group, wherein the alkylene group is optionally substituted with 1 to 4 substituents independently selected from R^b;

each R^5 and R^6 is independently hydrogen, alkyl, alkenyl, alkynyl, aryl, heteroaryl, cycloalkyl, or heterocyclyl; or R^5 and R^6 together with the carbon atom to which they are attached form a ring having from 5 to 7 ring atoms, wherein the ring optionally contains 1 or 2 heteroatoms in the ring independently selected from oxygen, sulfur or nitrogen;

wherein for R^1-R^6, each alkyl, alkenyl, and alkynyl is optionally substituted with R^x, or with 1, 2, 3, or 4 substituents independently selected from R^b; for R^1-R^6, each aryl and heteroaryl is optionally substituted with 1 to 4 substituents independently selected from R^c, and for R^1-R^6, each cycloalkyl and heterocyclyl is optionally substituted with 1 to 4 substituents independently selected from R^b and R^c;

each R^a is independently $-OR^d$, $-NO_2$, halo, $-S(O)_mR^d$, $-SR^d$, $-S(O)_2OR^d$, $-S(O)_mNR^dR^e$, $-NR^dR^e$, $-O(CR^fR^g)_nNR^dR^e$, $-C(O)R^d$, $-CO_2R^d$, $-CO_2(CR^fR^g)_nCONR^dR^e$, $-OC(O)R^d$, $-CN$, $-C(O)NR^dR^e$, $-NR^dC(O)R^e$, $-OC(O)NR^dR^e$, $-NR^dC(O)OR^e$, $-NR^dC(O)NR^dR^e$, $-CR^d(=N-OR^e)$, $-CF_3$, or $-OCF_3$;

each R^b is independently R^a, oxo or $=N-OR^e$;

each R^c is independently R^a, alkyl, alkenyl, or alkynyl; wherein each alkyl, alkenyl and alkynyl is optionally substituted with 1 to 4 substituents independently selected from R^b;

each R^d and R^e is independently hydrogen, alkyl, alkenyl, alkynyl, aryl, heteroaryl, cycloalkyl, or heterocyclyl; wherein each alkyl, alkenyl, alkynyl, aryl, heteroaryl, cycloalkyl and heterocyclyl is optionally substituted with 1 to 4 substituents independently selected from R^h; or R^d and R^e together with the atoms to which they are attached form a heterocyclic ring having from 5 to 7 ring atoms, wherein the heterocyclic ring optionally contains 1 or 2 additional heteroatoms independently selected from oxygen, sulfur or nitrogen;

each R^f and R^g is independently hydrogen, alkyl, aryl, heteroaryl, cycloalkyl, or heterocyclyl; wherein each alkyl, aryl, heteroaryl, cycloalkyl and heterocyclyl is optionally substituted with 1 to 4 substituents independently selected from R^h; or R^f and R^g together with the carbon atom to which they are attached form a ring having from 5 to 7 ring atoms, wherein the ring optionally contains 1 or 2 heteroatoms independently selected from oxygen, sulfur or nitrogen;

each R^h is independently halo, C_{1-6} alkyl, C_{1-6} alkoxy, aryl, (aryl)-C_{1-6} alkyl, heteroaryl, (heteroaryl)-C_{1-6} alkyl, hydroxy, amino, -NHC_{1-6} alkyl, -$N(C_{1-6}$ alkyl$)_2$, -$OC(O)C_{1-6}$ alkyl, -$C(O)C_{1-6}$ alkyl, -$C(O)OC_{1-6}$ alkyl, -$NHC(O)C_{1-6}$ alkyl, -$C(O)NHC_{1-6}$ alkyl, carboxy, nitro, -CN, or -CF_3;

R^k is hydrogen, alkyl, alkenyl, alkynyl, aryl, heteroaryl, cycloalkyl, or heterocyclyl; wherein each alkyl, alkenyl, alkynyl, aryl, heteroaryl, cycloalkyl and heterocyclyl is optionally substituted with 1 to 4 substituents independently selected from R^h;

R^m is hydrogen, alkyl, alkenyl, alkynyl, aryl, heteroaryl, cycloalkyl, or heterocyclyl; wherein each alkyl, alkenyl, alkynyl, aryl, heteroaryl, cycloalkyl and heterocyclyl is optionally substituted with 1 to 4 substituents independently selected from R^h;

each R^x is independently aryl, heteroaryl, cycloalkyl or heterocyclyl; wherein each aryl or heteroaryl is optionally substituted with 1 to 4 substituents selected from the group consisting of R^c, and wherein each cycloalkyl and heterocyclyl is optionally substituted with 1 to 4 substituents selected from R^b;

m is 0, 1, or 2;

n is 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10;

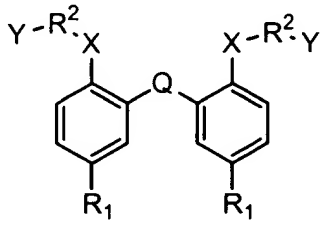
p is 1, 2, or 3;

r is 2, or 3; and

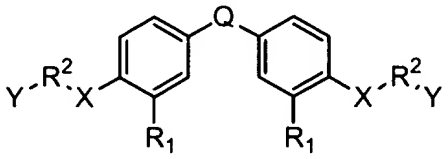
each *w* is independently 0, 1, 2, 3, or 4;

or a pharmaceutically-acceptable salt thereof.

41. A compound of formula XXIX or XXX:



(XXIX)



(XXX)

wherein:

Q is methylene;

each R^1 is chloro;

each R^2 is independently a covalent bond or alkylene; wherein alkylene is optionally substituted with 1 to 4 substituents independently selected from R^b;

each X is independently oxy (-O-) or -N(R^m)-;

each Y is independently NR^nR^p or a heterocyclyl containing at least one nitrogen atom, wherein each nitrogen of the heterocyclyl is substituted with R^3 or is linked to R^2, and wherein each heterocycle of Y is optionally substituted with 1, 2, 3, or 4 substituents independently selected from R^4;

each R^3 is independently hydrogen, alkyl, alkenyl, alkynyl, aryl, heteroaryl, cycloalkyl, oxo, or heterocyclyl; and each R^4 is independently alkyl, alkenyl, alkynyl, aryl, heteroaryl, cycloalkyl, heterocyclyl, or R^b; or R^3 and R^4 are joined to form a C_{1-4} alkylene group, wherein the alkylene group is optionally substituted with 1 to 4 substituents independently selected from R^b;

wherein for R^1-R^4, each alkyl, alkenyl, and alkynyl is optionally substituted with R^x, or with 1, 2, 3, or 4 substituents independently selected from R^b; for R^1-R^4, each aryl and heteroaryl is optionally substituted with 1 to 4 substituents independently selected from R^c, and for R^1-R^4, each cycloalkyl and heterocyclyl is optionally substituted with 1 to 4 substituents independently selected from R^b and R^c;

each R^a is independently $-OR^d$, $-NO_2$, halo, $-S(O)_mR^d$, $-SR^d$, $-S(O)_2OR^d$, $-S(O)_mNR^dR^e$, $-NR^dR^e$, $-O(CR^fR^g)_nNR^dR^e$, $-C(O)R^d$, $-CO_2R^d$, $-CO_2(CR^fR^g)_nCONR^dR^e$, $-OC(O)R^d$, -CN, $-C(O)NR^dR^e$, $-NR^dC(O)R^e$, $-OC(O)NR^dR^e$, $-NR^dC(O)OR^e$, $-NR^dC(O)NR^dR^e$, $-CR^d(=N-OR^e)$, $-CF_3$, or $-OCF_3$;

each R^b is independently R^a, oxo or $=N-OR^e$;

each R^c is independently R^a, alkyl, alkenyl, or alkynyl; wherein each alkyl, alkenyl and alkynyl is optionally substituted with 1 to 4 substituents independently selected from R^b;

each R^d and R^e is independently hydrogen, alkyl, alkenyl, alkynyl, aryl, heteroaryl, cycloalkyl, or heterocyclyl; wherein each alkyl, alkenyl, alkynyl, aryl, heteroaryl, cycloalkyl and heterocyclyl is optionally substituted with 1 to 4 substituents independently selected from R^h; or R^d and R^e together with the atoms to which they are attached form a heterocyclic ring having from 5 to 7 ring atoms, wherein the heterocyclic ring optionally contains 1 or 2 additional heteroatoms independently selected from oxygen, sulfur or nitrogen;

each R^f and R^g is independently hydrogen, alkyl, aryl, heteroaryl, cycloalkyl, or heterocyclyl; wherein each alkyl, aryl, heteroaryl, cycloalkyl and heterocyclyl is optionally substituted with 1 to 4 substituents independently selected from R^h; or R^f and R^g together with the carbon atom to which they are attached form a ring having from 5 to 7 ring atoms, wherein the ring optionally contains 1 or 2 heteroatoms independently selected from oxygen, sulfur or nitrogen;

each R^h is independently halo, C_{1-6} alkyl, C_{1-6} alkoxy, aryl, (aryl)-C_{1-6} alkyl, heteroaryl, (heteroaryl)-C_{1-6} alkyl, hydroxy, amino, $-NHC_{1-6}$ alkyl, $-N(C_{1-6}$ alkyl$)_2$, $-OC(O)C_{1-6}$ alkyl, $-C(O)C_{1-6}$ alkyl, $-C(O)OC_{1-6}$ alkyl, $-NHC(O)C_{1-6}$ alkyl, $-C(O)NHC_{1-6}$ alkyl, carboxy, nitro, -CN, or $-CF_3$;

R^m is hydrogen, alkyl, alkenyl, alkynyl, aryl, heteroaryl, cycloalkyl, or heterocyclyl; wherein each alkyl, alkenyl, alkynyl, aryl, heteroaryl, cycloalkyl and heterocyclyl is optionally substituted with 1 to 4 substituents independently selected from R^h;

each R^n and R^p is independently hydrogen, alkyl, alkenyl, alkynyl, aryl, heteroaryl, cycloalkyl, or heterocyclyl; wherein each alkyl, alkenyl, alkynyl, aryl, heteroaryl, cycloalkyl and heterocyclyl is optionally substituted with 1 to 4 substituents independently selected from R^h;

each R^x is independently aryl, heteroaryl, cycloalkyl or heterocyclyl; wherein each aryl or heteroaryl is optionally substituted with 1 to 4 substituents selected from the group consisting of R^c, and wherein each cycloalkyl and heterocyclyl is optionally substituted with 1 to 4 substituents selected from R^b;

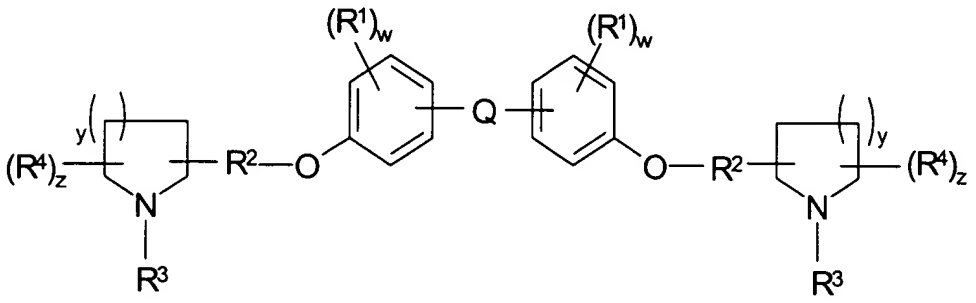
m is 0, 1, or 2; and

n is 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10;

or a pharmaceutically-acceptable salt thereof;

provided that when any Y is NR^nR^p or a nitrogen-linked heterocyclyl, then the R^2 attached to that Y is not a covalent bond or methylene.

42. The compound of claim 40 which is a compound of formula II:



(II)

wherein:

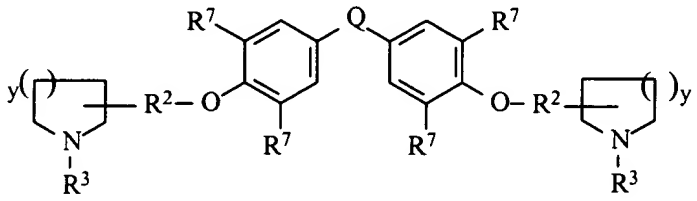
Q is -O-, $-S(O)_m-$, or $-CR^5R^6-$;

each *y* is independently 0, 1, 2, or 3; and

each *z* is independently 0, 1, 2, 3, or 4;

or a pharmaceutically-acceptable salt thereof.

43. The compound of claim 40 which is a compound of formula (III):



(III)

wherein

Q is -O-, -S(O)$_m$-, or -CR^{5}R^6-;

each R^7 is independently hydrogen, C$_{1-10}$ alkyl, C$_{2-10}$ alkenyl, C$_{2-10}$ alkynyl, cycloalkyl, or R^a;

each R^3 is independently hydrogen, C$_{1-10}$ alkyl, or oxo;

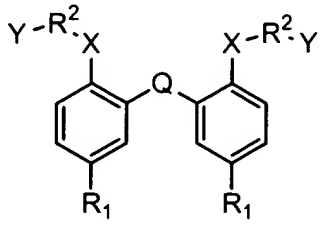
each R^5 and R^6 is independently hydrogen or C$_{1-10}$ alkyl; or R^5 and R^6 together with the carbon atom to which they are attached form a ring having from 5 to 7 ring atoms, wherein the ring optionally contains 1 or 2 heteroatoms in the ring independently selected from oxygen, sulfur and nitrogen;

wherein for R^3, R^5, R^6, and R^7, each alkyl, alkenyl, and alkynyl is optionally substituted with R^x, or with 1 to 4 substituents independently selected from R^b; and each cycloalkyl is optionally substituted with 1 to 4 substituents independently selected from R^b and R^c; and

each *y* is independently 1, 2, or 3;

or a pharmaceutically-acceptable salt thereof.

44. The compound a claim 40 which is a compound of formula XXIX:



(XXIX)

wherein:

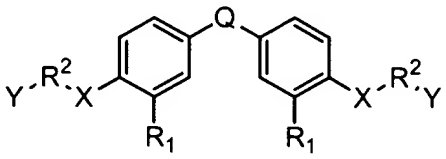
Q is methylene;

each R^1 is chloro;

each Y is independently a heterocyclyl containing at least one nitrogen atom, wherein each nitrogen of the heterocyclyl is substituted with R^3; and

and R^2 and X have any of the values defined in claim 1; or a pharmaceutically-acceptable salt thereof.

45. The compound a claim 40 which is a compound of formula XXX:



(XXX)

wherein:

Q is methylene;

each R^1 is chloro;

each Y is independently a heterocyclyl containing at least one nitrogen atom, wherein each nitrogen of the heterocyclyl is substituted with R^3; and

and R^2 and X have any of the values defined in claim 40; or a pharmaceutically-acceptable salt thereof.

46. The compound of claim 40 wherein each R^1 is independently C_{1-10} alkyl, C_{2-10} alkenyl, C_{2-10} alkynyl, cycloalkyl, or R^a.

47. The compound of claim 40 wherein each R^1 is independently C_{1-10} alkyl or halo.

48. The compound of claim 40 wherein each R^1 is independently methyl, ethyl, propyl, chloro, bromo, fluoro, or isopropyl.

49. The compound of claim 40 wherein each R^1 is independently methyl, or chloro.

50. The compound of claim 40 or 41 wherein each R^2 is independently a covalent bond or C_{1-10} alkylene.

51. The compound of claim 40 or 41 wherein each R^2 is independently a covalent bond, methylene, 1,2-ethylene, 1,3-propylene, (2R)-2-(methyl)ethane-1,2-diyl, (2S)-2-(methyl)ethane-1,2-diyl, 1-(methyl)butane-1,4-diyl, 1-(methyl)ethane-1,2-diyl, or 2,2-(dimethyl)propane-1,3-diyl.

52. The compound of claim 40 or 41 wherein each R^2 is independently a covalent bond, methylene, or ethylene.

53. The compound of claim 40 wherein Q is -O-, $-S(O)_m-$, or $-(CR^5R^6)_p-$.

54. The compound of claim 40 wherein Q is -O-, $-S(O)_m-$, or $-N(R^k)-$.

55. The compound of claim 40 wherein Q is $-(CR^5R^6)_p-$, or $-O(CR^5R^6)_rO-$.

56. The compound of claim 40 wherein Q is -O-, $-S(O)_m-$, $-(CR^5R^6)_p-$, or $-N(R^k)-$;

57. The compound of claim 40 wherein Q is methylene, 1,2-ethylene, 3,4-hexylene, dimethylmethylene, oxy, -NH-, $-OCH_2CH_2O-$, or a group $-C(R^5)(R^6)-$ wherein R^5 and R^6 together with the carbon to which they are attached form a cyclohexylene ring.

58. The compound of claim 40 or 41 wherein each X is oxy.

59. The compound of claim 40 or 41 wherein each X is -NH-.

60. The compound of claim 41 wherein each Y is independently NR^nR^p.

61. The compound of claim 41 wherein each Y is independently a heterocyclyl containing at least one nitrogen atom, wherein each nitrogen of the heterocyclyl is substituted with R^3 or linked to R^2, and wherein each heterocycle of Y is optionally substituted with 1, 2, 3, or 4 substituents independently selected from R^4.

62. The compound of claim 41 wherein each Y is independently a heterocyclyl containing at least one nitrogen atom, wherein each nitrogen of the heterocyclyl is linked to R^2, and wherein each heterocycle of Y is optionally substituted with 1, 2, 3, or 4 substituents independently selected from R^4.

63. The compound of claim 40 or 41 wherein each Y is independently a heterocyclyl selected from pyrrolidinyl, piperidinyl, and morpholinyl, wherein each heterocycle of Y is optionally substituted with 1, 2, 3, or 4 substituents independently selected from R^4.

64. The compound of claim 41 wherein Y is independently amino, diethylamino, dimethylamino, 1-methyl-4-piperidinyl, 1-methyl-3-piperidinyl, 1-methyl-2-piperidinyl, 4-piperidinyl, 3-piperidinyl, 2-piperidinyl, 1-isopropyl-3-pyrrolidinyl, morpholino, (2R,4R)-2-methoxycarbonyl-4-pyrrolidinyl, 1-methyl-3-pyrrolidinyl, 1-methyl-2-pyrrolidinyl, 3-pyrrolidinyl, 2-pyrrolidinyl, 1-pyrrolidinyl, (2S,4R)-2-methyl-4-pyrrolidinyl, (2R,4R)-2-carboxy-4-pyrrolidinyl, (2S,4S)-2-(N,N-dimethylamino)carbonyl-4-pyrrolidinyl, (2R,4R)-2-hydroxymethyl-4-pyrrolidinyl, or (2R,4R)-2-methoxymethyl-4-pyrrolidinyl.

65. The compound of claim 40 wherein each *w* is 0.

66. The compound of claim 40 wherein each *w* is 1.

67. The compound of claim 40 wherein each *w* is 2.

68. The compound of claim 42 or 43 wherein each *y* is independently 1 or 2.

69. The compound of claim 42 wherein each *z* is independently 0, 1, or 2.

70. The compound of claim 40 which is a compound of any one of formulae V-XXX, shown in Figures 1-3, wherein X, Y, Q, R^1, R^2, and w have the values given in claim 40.

71. The compound of claim 40, which is any one of compounds **1-11** shown in Table 1; or a pharmaceutically acceptable salt thereof.

72. A pharmaceutical composition comprising a compound as described in claim 40 or 41; and a pharmaceutically acceptable carrier.

73. A method of treating a disease or condition associated with sodium channel activity in a mammal, comprising administering to the mammal, a therapeutically effective amount of a pharmaceutical composition of claim 72.

74. The method of claim 73 wherein the disease or condition is neuropathic pain.